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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,796	07/06/2004	Gwong-Jen J Chang	6395-64909-02	5091

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KLARQUIST SPARKMAN, LLP
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EXAMINER

PARKIN, JEFFREY S

ART UNIT	PAPER NUMBER
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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/500,796	Applicant(s) CHANG, GWONG-JEN J	
	Examiner Jeffrey S. Parkin, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 December 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-54 is/are pending in the application.
- 4a) Of the above claim(s) 18-27, 29, 31, 33, 35 and 37-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-17, 28, 30, 32, 34, 36, 44-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Serial No.: 10/500,796
Applicant: Chang, G.

Docket No.: 6395-64909-02
Filing Date: 07/02/2004

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 14 December, 2007. Claims 1 and 3-54 are pending in the instant application. Claims 18-27, 29, 31, 33, 35, and 37-43 have been withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention. Claims 1, 3-17, 28, 30, 32, 34, 36, and 44-54 are currently under examination. A complete response to the final rejection must include cancellation of non-elected claims or other appropriate action (refer to 37 C.F.R. § 1.144 and M.P.E.P. § 821.01).

37 C.F.R. § 1.84

Acknowledgement is hereby made of receipt and entry of the drawing filed on 14 December, 2007, which is deemed to be acceptable.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 50-52 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in response to applicant's amendment.

35 U.S.C. § 101

The following is a quotation of 35 U.S.C. § 101 which reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

The previous rejection of claim 16 under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter, is hereby withdrawn in response to applicant's amendment.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The previous rejection of claims 1, 3, 8-10, 12, and 16 under 35 U.S.C. § 102(b) as being clearly anticipated by Pletnev *et al.* (1992), is hereby withdrawn in response to applicant's amendment.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102

of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-17, 28, 30, 32, 34, 36, and 44-54 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yasui *et al.* (1990) in view of Kochel *et al.* (2002), Ivy *et al.* (2000), Phillpotts *et al.* (1996), and Kozak (1987). The claims have been amended to incorporate a Japanese encephalitis virus (JEV) signal sequence as the signal sequence. Thus the claims are now directed toward a transcriptional unit comprising the JEV signal sequence and flavivirus antigen obtained from a non-JEV flavivirus or chimeric flavivirus antigen. The claims also stipulate that the constructs of interest have a CMV-IE promoter and Kozak consensus sequence. Additional limitations specify that the M/E proteins in the construct are obtained from a variety of art-recognized flaviviruses (e.g., West Nile virus, St. Louis encephalitis virus (SLE), Powassan virus, yellow fever virus, and dengue virus (serotypes 1, 2, 3, or 4). Further limitations specify that the construct encodes truncated forms of the E protein.

As previously set forth, Yasui and colleagues describe the preparation of recombinant baculovirus and vaccinia virus expression vectors encoding the prM, E, and NS1 proteins of the Japanese encephalitis virus (JEV). Expression cassettes were prepared comprising signal sequences and the respective genes

under the control of various promoters. The authors reported on page 663 (see Abstract) that "PrM and E proteins which had predictable signal sequences upstream on the N terminals were expressed with antigenically active form and molecular size the same as the authentic ones by the recombinant viruses. However, the recombinant viruses which had no such signal sequence expressed unprocessed proteins with antigenically denatured forms. These results suggest that normal proteolytic processing is needed to construct biologically active structures of JEV structural proteins." This teaching does not disclose constructs encoding a signal sequence from a first flavivirus and a second flavivirus immunogen.

Kochel and associates describe the preparation of nucleic acid dengue virus vaccines comprising a nucleic acid encoding the prM signal sequence and the envelope protein. These genes may be from the same isolate or different isolates. This teaching does not disclose the utilization of a JEV prM signal sequence or signal and antigen sequences from non-DEN coding regions.

Ivy and colleagues describe the preparation of nucleic acid constructs comprising a first nucleotide sequence encoding a signal sequence and a second nucleotide sequence encoding the E antigen of any given flavivirus (e.g., dengue, JEV, TBE, YFV, WNV, or SEV). The signal sequence may consist of either the htPA_L leader sequence or the prM leader sequence.

Philpotts and colleagues provide constructs comprising the CMV-IE promoter and SLE viral antigens.

Finally, Kozak provides consensus sequences for translational initiation.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was

made to prepare an expression cassette encoding the prM signal sequence and a flavivirus immunogen (e.g., Env) as taught by Yasui *et al.* (1990), and to substitute immunogenic sequences from other flaviviruses, as suggested by Kochel *et al.* (2002) and Ivy *et al.* (2000), since this expression cassette would provide a facile means for inducing immune responses against the flavivirus of interest. One of ordinary skill in the art would have also been motivated to employ the CMV-IE promoter and SLE immunogens of Phillpotts because the CMV-IE is an efficient promoter and SLE is a viable flavivirus target. One of ordinary skill in the art would have also been motivated to employ the ribosomal translational initiation sequences provided by Kozak since this would reasonably be expected to increase expression.

Response to Arguments

Applicants traverse and submit that none of the references suggest employing a JEV signal sequence in combination with an antigen from a second flavivirus, or employing a JEV signal sequence in combination with a chimeric antigen comprising sequences from two or more flaviviruses. It was also argued that the combination of references fails to provide a reasonable expectation of success. Applicant's arguments have been carefully considered but are deemed to be nonpersuasive. Kochel and colleagues clearly discuss and demonstrate the utility of multivalent flavivirus vaccines. The inventors clearly state (see col. 9, first full paragraph) that a multivalent dengue vaccine may be prepared by "cloning various combinations of the genes into **one** or more plasmid vectors." This teaching also discloses constructs comprising prM and E. Applicant correctly notes that this teaching does not disclose a construct comprising a JEV signal sequence and prM/E from

another flavivirus. However, Yasui and colleagues (1990) unequivocally demonstrate that inclusion of the JEV signal sequence produces immunogens that induce strong neutralizing and protective immune responses. Immunogens that lacked the signal sequences were considerably less efficient. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to incorporate the JEV signal sequence into an expression construct comprising a heterologous flavivirus prM/E coding region. There was more than a reasonable expectation of success because Yasui and colleagues clearly demonstrated that constructs carrying this sequence had favorable immunogenic properties (i.e., the induction of protective immune responses).

Nonstatutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 U.S.P.Q.2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 U.S.P.Q.2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 U.S.P.Q. 761 (C.C.P.A. 1982); *In re Vogel*, 422 F.2d 438, 164 U.S.P.Q. 619 (C.C.P.A. 1970); and *In re Thorington*, 418 F.2d 528, 163 U.S.P.Q. 644 (C.C.P.A. 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) or § 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. § 3.73(b).

Claims 1, 3, 8-10, 13-17, 28, 32, 34, 36, and 44 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 7,227,011. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '011 patent are directed toward an isolated nucleic acid comprising a transcriptional unit encoding a JEV signal sequence and immunogenic flavivirus antigen from a non-JEV flavivirus. Accordingly, this teaching meets all of the claimed limitations.

Action Is Final, Necessitated by Amendment

Applicant's amendment necessitated any and all new ground(s) of rejection presented in this Office action. Applicant is also reminded of their duty to disclose information material to patentability pursuant to 37 C.F.R. § 1.56. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908 or via e-mail at Jeffrey.Parkin@uspto.gov.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

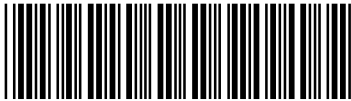
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin, Ph.D./
Primary Examiner, Art Unit 1648

23 March, 2008

<div>Application Number</div> <div></div>	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/500,796	CHANG, GWONG-JEN J	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	